We claim:

1. A method for cleaving single-stranded nucleic acid sequences at a desired location, the method comprising the steps of:

(i) contacting the nucleic acid with a single-stranded oligonucleotide, the oligonucleotide being functionally complementary to the nucleic acid in the region in which cleavage is desired and including a sequence that with its complement in the nucleic acid forms a restriction endonuclease recognition site that on restriction results in cleavage of the nucleic acid at the desired location; and

(ii) cleaving the nucleic acid solely at the recognition site formed by the complementation of the nucleic acid and the oligonucleotide;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the cleavage being carried out using a restriction endonuclease that is active at the chosen temperature.

2. A method for cleaving single-stranded nucleic acid sequences at a desired location, the method comprising the steps of:

(i) contacting the nucleic acid with a partially double-stranded oligonucleotide,

the single-stranded region of the oligonucleotide being functionally complementary to the nucleic acid in the region in which cleavage is desired, and the double-stranded region of the oligonucleotide having a restriction endonuclease recognition site; and

(ii) cleaving the nucleic acid solely at the restriction endonuclease recognition site formed by the complementation of the nucleic acid and the single-stranded region of the oligonucleotide;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the cleavage being carried out using a restriction endonuclease that is active at the chosen temperature.

3. In a method for displaying a member of a diverse family of peptides, polypeptides or proteins on the surface of a genetic package and collectively displaying at least a part of the diversity of the family, the improvement being characterized in that the displayed peptide, polypeptide or protein is encoded at least in part by a nucleic acid that has been cleaved at a desired location by a method comprising the steps of:

(i) contacting the nucleic acid with a single-stranded oligonucleotide, the

oligonucleotide being functionally complementary to the nucleic acid in the region in which cleavage is desired and including a sequence that with its complement in the nucleic acid forms a restriction endonuclease recognition site that on restriction results in cleavage of the nucleic acid at the desired location; and

(ii) cleaving the nucleic acid solely at the recognition site formed by the complementation of the nucleic acid and the oligonucleotide;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the cleavage being carried out using a restriction endonuclease that is active at the chosen temperature.

4. In a method for displaying a member of a diverse family of peptides, polypeptides or proteins on the surface of a genetic package and collectively displaying at least a part of the diversity of the family, the improvement being characterized in that the displayed peptide, polypeptide or protein is encoded by a DNA sequence comprising a nucleic acid that has been cleaved at a desired location by

(i) contacting the nucleic acid with a partially double-stranded oligonucleotide, the single-stranded region of the

oligonucleotide being functionally complementary to the nucleic acid in the region in which cleavage is desired, and the double-stranded region of the oligonucleotide having a restriction endonuclease recognition site; and

(ii) cleaving the nucleic acid solely at the restriction endonuclease recognition cleavage site formed by the complementation of the nucleic acid and the single-stranded region of the oligonucleotide;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the cleavage being carried out using a restriction endonuclease that is active at the chosen temperature.

5. A method for displaying a member of a diverse family of peptides, polypeptides or proteins on the surface of a genetic package and collectively displaying at least a part of the diversity of the family, the method comprising the steps of:

(i) preparing a collection of nucleic acids that code at least in part for members of the diverse family;

(ii) rendering the nucleic acids single-stranded;

(iii) cleaving the single-stranded nucleic acids at a desired location by a method comprising the steps of:

(a) contacting the nucleic acid with a single-stranded oligonucleotide, the oligonucleotide being functionally complementary to the nucleic acid in the region in which cleavage is desired and including a sequence that with its complement in the nucleic acid forms a restriction endonuclease recognition site that on restriction results in cleavage of the nucleic acid at the desired location; and

(b) cleaving the nucleic acid solely at the recognition site formed by the complementation of the nucleic acid and the oligonucleotide;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the cleavage being carried out using a restriction endonuclease that is active at the chosen temperature; and

(iv) displaying a member of the family of peptides, polypeptides or proteins coded, at least in part, by the cleaved nucleic acids on the surface of the genetic package and collectively displaying at least a portion of the diversity of the family.

6. A method for displaying a member of a diverse family of peptides, polypeptides or proteins on the surface of a genetic package and collectively displaying at least a portion of the diversity of the family, the method comprising the steps of:

(i) preparing a collection of nucleic acids that code, at least in part, for members of the diverse family;

(ii) rendering the nucleic acids single-stranded;

(iii) cleaving the single-stranded nucleic acids at a desired location by a method comprising the steps of:

(a) contacting the nucleic acid with a partially double-stranded oligonucleotide, the single-stranded region of the oligonucleotide being functionally complementary to the nucleic acid in the region in which cleavage is desired, and the double-stranded region of the oligonucleotide having a restriction endonuclease recognition site; and

(b) cleaving the nucleic acid solely at the restriction endonuclease recognition cleavage site formed by the complementation of the nucleic acid and the single-stranded region of the oligonucleotide;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the

chosen temperature and at the desired location, and the restriction being carried out using a cleavage endonuclease that is active at the chosen temperature; and

(iv) displaying a member of the family of peptides, polypeptides or proteins coded, at least in part, by the cleaved nucleic acids on the surface of the genetic package and collectively displaying at least a portion of the diversity of the family.

7. In a method for expressing a member of a diverse family of peptides, polypeptides or proteins and collectively expressing at least a part of the diversity of the family, the improvement being characterized in that the expressed peptide, polypeptide or protein is encoded at least in part by a nucleic acid that has been cleaved at a desired location by a method comprising the steps of:

(i) contacting the nucleic acid with a single-stranded oligonucleotide, the oligonucleotide being functionally complementary to the nucleic acid in the region in which cleavage is desired and including a sequence that with its complement in the nucleic acid forms a restriction endonuclease recognition site that on restriction results in cleavage of the nucleic acid at the desired location; and

(ii) cleaving the nucleic acid solely at the recognition site formed by the complementation of the nucleic acid and the oligonucleotide;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the cleavage being carried out using a restriction endonuclease that is active at the chosen temperature.

8. In a method for expressing a member of a diverse family of peptides, polypeptides or proteins and collectively expressing at least a part of the diversity of the family, the improvement being characterized in that the expressed peptide, polypeptide or protein is encoded by a DNA sequence comprising a nucleic acid that has been cleaved at a desired location by

(i) contacting the nucleic acid with a partially double-stranded oligonucleotide, the single-stranded region of the oligonucleotide being functionally complementary to the nucleic acid in the region in which cleavage is desired, and the double-stranded region of the oligonucleotide having a restriction endonuclease recognition site; and

(ii) cleaving the nucleic acid solely at the restriction endonuclease recognition cleavage site formed by the complementation of the nucleic acid and the single-stranded region of the oligonucleotide;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the cleavage being carried out using a restriction endonuclease that is active at the chosen temperature.

9. A method for expressing a member of a diverse family of peptides, polypeptides or proteins and collectively expressing at least a part of the diversity of the family, the method comprising the steps of:

(i) preparing a collection of nucleic acids that code at least in part for members of the diverse family;

(ii) rendering the nucleic acids single-stranded;

(iii) cleaving the single-stranded nucleic acids at a desired location by a method comprising the steps of:

(a) contacting the nucleic acid with a single-stranded oligonucleotide, the oligonucleotide being functionally complementary to the nucleic acid in the region in which cleavage is desired and including a sequence that with its complement in the nucleic acid forms a restriction endonuclease recognition site that on restriction results in cleavage of the nucleic acid at the desired location; and

(b) cleaving the nucleic acid solely at the recognition site formed by the complementation of the nucleic acid and the oligonucleotide;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the cleavage being carried out using a restriction endonuclease that is active at the chosen temperature; and

(iv) expressing a member of the family of peptides, polypeptides or proteins coded, at least in part, by the cleaved nucleic acids and collectively expressing at least a portion of the diversity of the family.

10. A method for expressing a member of a diverse family of peptides, polypeptides or proteins and collectively expressing at least a portion of the diversity of the family, the method comprising the steps of:

(i) preparing a collection of nucleic acids that code, at least in part, for members of the diverse family;

(ii) rendering the nucleic acids single-stranded;

(iii) cleaving the single-stranded nucleic acids at a desired location by a method comprising the steps of:

(a) contacting the nucleic acid with a partially double-stranded oligonucleotide, the single-stranded region of the oligonucleotide being functionally complementary to the nucleic acid in the region in which cleavage is desired, and the double-stranded region of the oligonucleotide having a restriction endonuclease recognition site; and

(b) cleaving the nucleic acid solely at the restriction endonuclease recognition cleavage site formed by the complementation of the nucleic acid and the single-stranded region of the oligonucleotide;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the restriction being carried out using a cleavage endonuclease that is active at the chosen temperature; and

(iv) expressing a member of the family of peptides, polypeptides or proteins coded, at least in part, by the cleaved nucleic acids and collectively expressing at least a portion of the diversity of the family.

11. A library comprising a collection of genetic packages that display a member of a diverse family of peptides, polypeptides or proteins and

collectively display at least a portion of the diversity of the family, the library being produced using the methods of claims 3, 4, 5 or 6.

12. A library comprising a collection of genetic packages that display a member of a diverse family of peptides, polypeptides or proteins and that collectively display at least a portion of the family, the displayed peptides, polypeptides or proteins being encoded by DNA sequences comprising at least in part sequences produced by cleaving single-stranded nucleic acid sequences at a desired location by a method comprising the steps of:

(i) contacting the nucleic acid with a single-stranded oligonucleotide, the oligonucleotide being functionally complementary to the nucleic acid in the region in which cleavage is desired and including a sequence that with its complement in the nucleic acid forms a restriction endonuclease recognition site that on restriction results in cleavage of the nucleic acid at the desired location; and

(ii) cleaving the nucleic acid solely at the recognition site formed by the complementation of the nucleic acid and the oligonucleotide;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur

at the chosen temperature and at the desired location, and the cleavage being carried out using a restriction endonuclease that is active at the chosen temperature.

13. A library comprising a collection of genetic packages that display a member of a diverse family of peptides, polypeptides or proteins and that collectively display at least a portion of the diversity of the family of the displayed peptides, polypeptides or proteins being encoded by DNA sequences comprising at least in part sequences produced by cleaving single-stranded nucleic acid sequences at a desired location by a method comprising the steps of:

(i) contacting the nucleic acid with a partially double-stranded oligonucleotide, the single-stranded region of the oligonucleotide being functionally complementary to the nucleic acid in the region in which cleavage is desired, and the double-stranded region of the oligonucleotide having a restriction endonuclease recognition site; and

(ii) cleaving the nucleic acid solely at the restriction endonuclease recognition cleavage site formed by the complementation of the nucleic acid and the single-stranded region of the oligonucleotide;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location,

and the cleavage being carried out using a restriction endonuclease that is active at the chosen temperature.

14. A library comprising a collection of members of a diverse family of peptides, polypeptides or proteins and collectively comprising at least a portion of the diversity of the family, the library being produced using the methods of claims 7, 8, 9 or 10.

15. A library comprising a collection of members of a diverse family of peptides, polypeptides or proteins and collectively comprising at least a portion of diversity of the family, the peptides, polypeptides or proteins being encoded by DNA sequences comprising at least in part sequences produced by cleaving single-stranded nucleic acid sequences at a desired location by a method comprising the steps of:

(i) contacting the nucleic acid with a single-stranded oligonucleotide, the oligonucleotide being functionally complementary to the nucleic acid in the region in which cleavage is desired and including a sequence that with its complement in the nucleic acid forms a restriction endonuclease recognition site that on restriction results in cleavage of the nucleic acid at the desired location; and

(ii) cleaving the nucleic acid solely at the recognition site formed by the complementation of the nucleic acid and the oligonucleotide;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the cleavage being carried out using a restriction endonuclease that is active at the chosen temperature.

16. A library comprising a collection of members of a diverse family of peptides, polypeptides or proteins and collectively comprising at least a portion of the diversity of the family, the peptides, polypeptides or proteins being encoded by DNA sequences comprising at least in part sequences produced by cleaving single-stranded nucleic acid sequences at a desired location by a method comprising the steps of:

(i) contacting the nucleic acid with a partially double-stranded oligonucleotide, the single-stranded region of the oligonucleotide being functionally complementary to the nucleic acid in the region in which cleavage is desired, and the double-stranded region of the oligonucleotide having a restriction endonuclease recognition site; and

(ii) cleaving the nucleic acid solely at the restriction endonuclease recognition cleavage site formed by the complementation of the nucleic acid and the single-stranded region of the oligonucleotide;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic

acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the cleavage being carried out using a restriction endonuclease that is active at the chosen temperature.

17. A library of claims 11, 12 or 13 wherein the genetic packages are selected from the group of phage, phagemid or yeast.

18. A library of claims 17 wherein the genetic packages are selected are phage or phagemid.

19. The methods or libraries according claims 2, 4, 6, 8, 10, 13 or 16 wherein in the restriction endonuclease recognition site is for a Type II-S restriction endonuclease.

20. The methods or libraries according to claims 1 to 19, wherein the nucleic acid is cDNA.

21. The methods or libraries according to any one of claims 1 to 20, wherein the nucleic acids encode at least a portion of an immunoglobulin.

22. The methods or libraries according to claim 21, wherein the immunoglobulin comprises a Fab or single chain Fv.

23. The methods or libraries according to claim 21 or 22, wherein the immunoglobulin comprises at least portion of a heavy chain.

24. The method or libraries according to claim 23, wherein the heavy chain is IgM, IgG, IgA, IgE or IgD.

25. The methods or libraries according to claim 23 or 24, wherein at least a portion of the heavy chain is human.

26. The methods or libraries according to claim 21 or 22, wherein the immunoglobulin comprises at least a portion of FR1.

27. The methods or libraries according to claim 26, wherein at least a portion of the FR1 is human.

28. The methods or libraries according to claim 21 or 22, wherein the immunoglobulin comprises at least a portion of a light chain.

29. The methods or libraries according to claim 28, wherein at least a portion of the light chain is human.

30. The methods or libraries according to any one of claims 1 to 16, wherein the nucleic acid sequences are at least in part derived from patients suffering from at least one autoimmune disease and/or cancer.

31. The methods or libraries according to claim 30, wherein the autoimmune disease is selected from the group comprising lupus, erythematosus,

systemic sclerosis, rheumatoid arthritis, antiphosolipid syndrome or vasculitis.

32. The methods or libraries according to claim 30, wherein the nucleic acids are at least in part isolated from the group comprising peripheral blood cells, bone marrow cells spleen cells or lymph node cells.

33. The methods according to claim 5, 6, 9 or 10 further comprising at least one nucleic acid amplification step between one or more of steps (i) and (ii), steps (ii) and (iii) or between steps (iii) and (iv).

34. The method according to claim 33, wherein amplification primers for the amplification step are functionally complementary to a constant region of the nucleic acids.

35. The method according to claim 34, wherein the constant region is genetically constant in the nucleic acids.

36. The method according to claim 35, wherein the genetically constant region is a part of the genome of immunoglobulin genes selected from the group of IgM, IgG, IgA, IgE or IgD.

37. The method according to claim 34, wherein the constant region is exogenous to the nucleic acids.

38. The methods according to claim 33, wherein the amplification step uses geneRACE™.

39. The methods or libraries according to any one of claims 1 to 16, wherein the chosen temperature is between 37°C and 75°C

40. The methods or libraries according to claim 39, wherein the chosen temperature is between 45°C and 75°C.

41. The methods or libraries according to claim 40, wherein the chosen temperature is between 50°C and 60°C.

42. The methods or libraries according to claim 41, wherein the chosen temperature is between 55°C and 60°C.

43. The methods or libraries according to claim 1, 3, 5, 7, 9, 12 or 15, wherein the length of the single-stranded oligonucleotide is between 17 and 30 bases.

44. The methods or libraries according to claim 43, wherein the length of the single-stranded oligonucleotide is between 18 and 24 bases.

45. The methods or libraries according to claim 1, 3, 5, 7, 9, 12 or 15, wherein the restriction endonuclease is selected from the group comprising *Mae*III, *Tsp*45I, *Hph*I, *Bsa*JI, *Alu*I, *Blp*I, *Dde*I, *Bgl*II, *Msl*I, *Bsi*EI, *Eae*I, *Eag*I, *Hae*III, *Bst*4CI, *Hpy*CH4III, *Hinf*I, *Mly*I, *Ple*I, *Mnl*I, *Hpy*CH4V, *Bsm*AI, *Bpm*I, *Xmn*I, or *Sac*I.

46. The methods or libraries according to claim 45, wherein the restriction endonuclease is selected from the group comprising *Bst*4CI, *Taa*I, *HpyCH4*III, *Blp*I, *Hpy*CH4V or *Msl*I.

47. The methods or libraries according to claim 2, 4, 6, 8, 10, 13 or 16, wherein the length of the single-stranded region of the partially double-stranded oligonucleotide is between 14 and 22 bases.

48. The methods or libraries according to claim 47, wherein the length of the single-stranded region of the partially double-stranded oligonucleotide is between 14 and 17 bases.

49. The methods or libraries according to claim 47, wherein the length of the single-stranded region of the oligonucleotide is between 18 and 20 bases.

50. The methods or libraries according to claim 2, 4, 6, 8, 10, 13 or 16, wherein the length of the double-stranded region of the partially double-stranded oligonucleotide is between 10 and 14 base pairs formed by a stem and its palindrome.

51. The methods or libraries according to claim 50 wherein, the partially double-stranded oligonucleotide comprises a loop of 3 to 8 bases between the stem and the palindrome.

52. The methods or libraries according to claim 19 wherein the Type II-S restriction endonuclease

is selected from the group comprising AarICAC, AceIII, Bbr7I, BbvI, BbvII, Bce83I, BceAI, BcefI, BciVI, BfiI, BinI, BscAI, BseRI, BsmFI, BspMI, EciI, Eco57I, FauI, FokI, GsuI, HgaI, HphI, MboII, MlyI, MmeI, MnlI, PleI, RleAI, SfaNI, SspD5I, Sth132I, StsI, TaqII, Tth111II, or UbaPI.

53. The methods or libraries according to claim 52, wherein the Type II-S restriction endonuclease is *Fok*I.

54. A method for preparing single-stranded nucleic acids, the method comprising the steps of:

(i) contacting a single-stranded nucleic acid sequence that has been cleaved with a restriction endonuclease with a partially double-stranded oligonucleotide, the single-stranded region of the oligonucleotide being functionally complementary to the nucleic acids in the region that remains after cleavage, the double-stranded region of the oligonucleotide including any sequences necessary to return the sequences that remain after cleavage into proper and original reading frame for expression and containing a restriction endonuclease recognition site 5' of those sequences; and

(ii) cleaving the partially double-stranded oligonucleotide sequence solely at the restriction endonuclease recognition site contained within the double-stranded region of the partially double-stranded oligonucleotide.

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the cleavage being carried out using a restriction endonuclease that is active at the chosen temperature.

55. The method according to claim 54, wherein the length of the single-stranded portion of the partially double-stranded oligonucleotide is between 2 and 15 bases.

56. The method according to claim 55, wherein the length of the single-stranded portion of the partially double-stranded oligonucleotide is between 7 and 10 bases.

57. The method according to claim 54, wherein the length of the double-stranded portion of the partially double-stranded oligonucleotide is between 12 and 100 base pairs.

58. The method according to claim 57, wherein the length of the double-stranded portion of the partially double-stranded oligonucleotide is between 20 and 100 base pairs.

59. A method for preparing a library comprising a collection of genetic packages that display a member of a diverse family of peptides,

polypeptides or proteins and that collectively display at least a portion of the family comprising the steps:

(i) preparing a collection of nucleic acids that code at least in part for members of the diverse family;

(ii) rendering the nucleic acids single-stranded;

(iii) cleaving the single-stranded nucleic acids at a desired location by a method comprising the steps of:

(a) contacting the nucleic acid with a single-stranded oligonucleotide, the oligonucleotide being functionally complementary to the nucleic acid in the region in which cleavage is desired and including a sequence that with its complement in the nucleic acid forms a restriction endonuclease recognition site that on restriction results in cleavage of the nucleic acid at the desired location; and

(b) cleaving the nucleic acid solely at the recognition site formed by the complementation of the nucleic acid and the oligonucleotide;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the cleavage being carried out using a

restriction endonuclease that is active at the chosen temperature;

(iv) contacting the nucleic acid with a partially double-stranded oligonucleotide, the single-stranded region of the oligonucleotide being functionally complementary to the nucleic acids in the region that remains after the cleavage in step (iii) has been effected, and the double-stranded region of the oligonucleotide including any sequences necessary to return the sequences that remain after cleavage into proper and original reading frame for display and containing a restriction endonuclease recognition site 5' of those sequences that is different from the restriction site used in step (iii); and

(v) cleaving the nucleic acid solely at the restriction endonuclease recognition cleavage site contained within the double-stranded region of the partially double-stranded oligonucleotide;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the restriction being carried out using a cleavage endonuclease that is active at the chosen temperature; and

(vi) displaying a member of the family of peptides, polypeptides or proteins coded, at least in part, by the cleaved nucleic acids on the surface of the genetic package and collectively displaying at least a portion of the diversity of the family.

60. A method for preparing a library comprising a collection of members of a diverse family of peptides, polypeptides or proteins and collectively comprising at least a portion of the family comprising the steps:

(i) preparing a collection of nucleic acids that code at least in part for members of the diverse family;

(ii) rendering the nucleic acids single-stranded;

(iii) cleaving the single-stranded nucleic acids at a desired location by a method comprising the steps of:

(a) contacting the nucleic acid with a single-stranded oligonucleotide, the oligonucleotide being functionally complementary to the nucleic acid in the region in which cleavage is desired and including a sequence that with its complement in the nucleic acid forms a restriction endonuclease recognition site that on restriction results in cleavage of the nucleic acid at the desired location; and

(b) cleaving the nucleic acid solely at the recognition site formed by the complementation of the nucleic acid and the oligonucleotide;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the

chosen temperature and at the desired location, and the cleavage being carried out using a restriction endonuclease that is active at the chosen temperature;

(iv) contacting the nucleic acid with a partially double-stranded oligonucleotide, the single-stranded region of the oligonucleotide being functionally complementary to the nucleic acids in the region that remains after the cleavage in step (iii) has been effected, and the double-stranded region of the oligonucleotide including any sequence necessary to return the sequences that remain after cleavage into proper and original reading frame for expression and containing a restriction endonuclease recognition site 5' of those sequences that is different from the restriction site used in step (iii); and

(v) cleaving the nucleic acid solely at the restriction endonuclease recognition cleavage site contained within the double-stranded region of the partially double-stranded oligonucleotide;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the restriction being carried out using a cleavage endonuclease that is active at the chosen temperature; and

(vi) expressing a member of the family of peptides, polypeptides or proteins coded, at least in part, by the cleaved nucleic acids and collectively

expressing at least a portion of the diversity of the family.

61. The methods according to claim 59 or 60, further comprising at least one nucleic acid amplification step between one or more of steps (i) and (ii), steps (ii) and (iii), steps (iii) and (iv) and steps (iv) and (v).

62. A library comprising a collection of genetic packages that display a member of a diverse family of peptides, polypeptides or proteins and collectively display at least a portion of the diversity of the family, the library being produced using the methods of claims 59 or 61.

63. A library comprising a collection of members of a diverse family of peptides, polypeptides or proteins and collectively comprise at least a portion of the diversity of the family, the library being produced using the methods of claims 60 or 61.

64. The methods and libraries according to any one of claim 59 to 63, wherein the members of the library encode immunoglobulins.

65. The method and libraries according to claim 64, wherein the double-stranded region of the oligonucleotide encodes at least a part of a framework sequence of an immunoglobulin.

66. The method and libraries according to claim 65, wherein the framework sequence comprises framework 1 of an antibody.

67. The method and libraries according to claim 66, wherein the framework sequence comprises framework 1 of a variable domain of a light chain.

68. The method and libraries according to claim 66, wherein the framework sequence comprises framework 1 of a variable domain of a heavy chain.

69. The method and libraries according to claim 65, wherein the framework sequence comprises framework 3 of an antibody.

70. The method and libraries according to claim 69, wherein the framework sequence comprises framework 3 of a variable domain of a light chain.

71. The method and libraries according to claim 69, wherein the framework sequence is framework 3 of a variable domain of a heavy chain.

72. The method and libraries according to claim 66, wherein the 5' primer is complementary to a region outside framework 1.

73. The method according to claim 61, wherein amplification primers for the amplification step are functionally complementary to a constant region of the nucleic acids.

74. The method according to claim 73, wherein the constant region is genetically constant in the nucleic acids.

75. The method according to claim 74, wherein the genetically constant region is part of the genome of immunoglobulin genes selected from the group of IgM, IgG, IgA, IgE or IgD.

76. The method according to claim 73, wherein the constant region is exogenous to the nucleic acids.

77. The methods according to claim 61, wherein the amplification step uses geneRACE™.

78. A vector comprising:

(i) a DNA sequence encoding an antibody variable region linked to a version of PIII anchor which does not mediate infection of phage particles; and

(ii) wild-type gene III.

79. The vector according to claim 78, wherein the DNA encodes a Fab.

80. The vector according to claim 78, wherein the DNA encodes heavy chain VHCH1.

81. The vector according to claim 80, wherein the heavy chain VHCH1 is linked to trpIII.

82. The vector according to claim 78, wherein the DNA encodes light chain VLCL.

83. The vector according to claim 82, wherein the light chain VLCL is linked to trpIII.

84. The vector according to claim 78, wherein the DNA encodes scFv.

85. The vector according to claim 84, wherein the scFv is VL-VH.

86. The vector according to claim 84, wherein the scFv is VH-VL.

87. The vector according to claim 78, wherein the DNA sequence encoding an antibody variable region linked to a version of PIII anchor further comprises an inducible promoter.

88. The vector according to claim 87, wherein the inducible promoter regulates expression of the DNA sequence encoding an antibody variable region linked to a version of PIII anchor.

89. The vector according to claim 78, wherein the DNA sequence encoding an antibody variable region linked to a version of PIII anchor further comprises an amber stop codon.

90. The vector according to claim 89, wherein the DNA encoding the amber stop codon is located between the antibody variable region and the version of pIII.

91. The vector according to any one of claims 78 to 90 wherein the vector is phage or phagemid.

92. A method for producing a population of immunoglobulin genes that comprises steps of:

(i) introducing synthetic diversity into at least one of CDR1 or CDR2 of those genes; and

(ii) combining the diversity from step (i) with CDR3 diversity captured from B cells.

93. The method according to claim 92, wherein synthetic diversity is introduced into both CDR1 and CDR2.

94. A method for producing a library of immunoglobulin genes that comprises

(i) introducing synthetic diversity into at least one of CDR1 or CDR2 of those genes; and

(ii) combining the diversity from step (i) with CDR3 diversity captured from B cells.

95. The method according to claim 94, wherein synthetic diversity is introduced into both CDR1 and CDR2.

96. A library of immunoglobulins that comprise members with at least one variable domain in which at least one of CDR1 and CDR2 contain synthetic diversity and CDR3 diversity is captured from B cells.

97. A library according to claim 96, where both CDR1 and CDR2 contain synthetic diversity.

98. The vector according to claim 78, wherein the version of PIII anchor is characterized by a wild type amino acid sequence and is encoded by a non-wild type degenerate DNA sequence to a very high extent.

99. In a method for displaying a member of a diverse family of peptides, polypeptides or proteins on the surface of a genetic package and collectively displaying at least a part of the diversity of the family, the improvement being characterized in that the displayed peptide, polypeptide or protein is encoded by a DNA sequence comprising a nucleic acid that has been cleaved at a desired location by

(i) contacting the nucleic acid with a partially double-stranded oligonucleotide, the single-stranded region of the oligonucleotide being functionally complementary to the nucleic acid at its 5' terminal and

(ii) cleaving the nucleic acid solely at a restriction endonuclease cleavage site located in the double-stranded region of the oligonucleotide or amplifying the nucleic acid using a primer at least in part functionally complementary to at least a part of the double-stranded region of the oligonucleotide, the primer also introducing on amplification an endonuclease cleavage site and cleaving the amplified nucleic acid sequence solely at that site;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic

acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the cleavage being carried out using a restriction endonuclease that is active at the chosen temperature.

100. A method for displaying a member of a diverse family of peptides, polypeptides or proteins on the surface of a genetic package and collectively displaying at least a portion of the diversity of the family, the method comprising the steps of:

(i) preparing a collection of nucleic acids that code, at least in part, for members of the diverse family;

(ii) rendering the nucleic acids single-stranded;

(iii) cleaving the single-stranded nucleic acids at a desired location by a method comprising the steps of:

(a) contacting the nucleic acid with a partially double-stranded oligonucleotide, the single-stranded region of the oligonucleotide being functionally complementary to the nucleic acid at its 5' terminal region; and

(b) cleaving the nucleic acid solely at a restriction endonuclease cleavage site located in the double-stranded region of the oligonucleotide or amplifying the nucleic acid using a primer at least in part functionally complementary to at least a part of the double-stranded region of the

oligonucleotide, the primer also introducing on amplification an endonuclease cleavage site and cleaving the amplified nucleic acid sequence solely at that site;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the restriction being carried out using a cleavage endonuclease that is active at the chosen temperature; and

(iv) displaying a member of the family of peptides, polypeptides or proteins coded, at least in part, by the cleaved nucleic acids on the surface of the genetic package and collectively displaying at least a portion of the diversity of the family.

101. In a method for expressing a member of a diverse family of peptides, polypeptides or proteins and collectively expressing at least a part of the diversity of the family, the improvement being characterized in that the expressed peptide, polypeptide or protein is encoded by a DNA sequence comprising a nucleic acid that has been cleaved at a desired location by

(i) contacting the nucleic acid with a partially double-stranded oligonucleotide, the single-stranded region of the oligonucleotide being functionally

complementary to the nucleic acid at its 5' terminal region; and

(ii) cleaving the nucleic acid solely at the restriction endonuclease cleavage site located in the double-stranded region of the oligonucleotide or amplifying the nucleic acid using a primer at least in part functionally complementary to at least a part of the double-stranded region of the oligonucleotide, the primer also introducing on amplification an endonuclease cleavage site and cleaving the amplified nucleic acid sequence solely at that site;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the cleavage being carried out using a restriction endonuclease that is active at the chosen temperature.

102. A method for expressing a member of a diverse family of peptides, polypeptides or proteins and collectively expressing at least a portion of the diversity of the family, the method comprising the steps of:

(i) preparing a collection of nucleic acids that code, at least in part, for members of the diverse family;

(ii) rendering the nucleic acids single-stranded;

(iii) cleaving the single-stranded nucleic acids at a desired location by a method comprising the steps of:

(a) contacting the nucleic acid with a partially double-stranded oligonucleotide, the single-stranded region of the oligonucleotide being functionally complementary to the nucleic acid at its 5' terminal region; and

(b) cleaving the nucleic acid solely at a restriction endonuclease cleavage site located in the double-stranded region of the nucleotide; or amplifying the nucleic acid using a primer at least in part functionally complementary to at least a part of the double-stranded region of the oligonucleotide, the primer also introducing on amplification an endonuclease cleavage site and cleaving the amplified nucleic acid sequence solely at that site;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the restriction being carried out using a cleavage endonuclease that is active at the chosen temperature; and

(iv) expressing a member of the family of peptides, polypeptides or proteins coded, at least in part, by the cleaved nucleic acids and collectively expressing at least a portion of the diversity of the family.

103. A method for preparing a library comprising a collection of genetic packages that display a member of a diverse family of peptides, polypeptides or proteins and that collectively display at least a portion of the family comprising the steps:

(i) preparing a collection of nucleic acids that code at least in part for members of the diverse family;

(ii) rendering the nucleic acids single-stranded;

(iii) cleaving the single-stranded nucleic acids at a desired location by a method comprising the steps of:

(a) contacting the nucleic acid with a single-stranded oligonucleotide, the oligonucleotide being functionally complementary to the nucleic acid in the region in which cleavage is desired and including a sequence that with its complement in the nucleic acid forms a restriction endonuclease recognition site that on restriction results in cleavage of the nucleic acid at the desired location; and

(b) cleaving the nucleic acid solely at the recognition site formed by the complementation of the nucleic acid and the oligonucleotide;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the cleavage being carried out using a restriction endonuclease that is active at the chosen temperature;

(iv) contacting the nucleic acid with a partially double-stranded oligonucleotide, the single-stranded region of the oligonucleotide being functionally complementary to the nucleic acids in the 5' terminal region that remains after the cleavage in step (iii) has been effected, and the double-stranded region of the oligonucleotide including any sequences necessary to return the sequences that remain after cleavage into proper and original reading frame for display; and

(v) cleaving the nucleic acid solely at a restriction endonuclease cleavage site contained within the double-stranded region of the partially double-stranded oligonucleotide, the site being different from that used in step (iii) or amplifying the nucleic acid using a primer at least in part functionally complementary to at least a part of the double-stranded region of the oligonucleotide, the primer also introducing on amplification an endonuclease cleavage site and cleaving the amplified nucleic acid sequence solely at that site;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain

the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the restriction being carried out using a cleavage endonuclease that is active at the chosen temperature; and

(vi) displaying a member of the family of peptides, polypeptides or proteins coded, at least in part, by the cleaved nucleic acids on the surface of the genetic package and collectively displaying at least a portion of the diversity of the family.

104. A method for preparing a library comprising a collection of members of a diverse family of peptides, polypeptides or proteins and collectively comprising at least a portion of the family comprising the steps:

(i) preparing a collection of nucleic acids that code at least in part for members of the diverse family;

(ii) rendering the nucleic acids single-stranded;

(iii) cleaving the single-stranded nucleic acids at a desired location by a method comprising the steps of:

(a) contacting the nucleic acid with a single-stranded oligonucleotide, the oligonucleotide being functionally complementary to the nucleic acid in the region in which cleavage is desired and including a sequence that with its complement

in the nucleic acid forms a restriction endonuclease recognition site that on restriction results in cleavage of the nucleic acid at the desired location; and

(b) cleaving the nucleic acid solely at the recognition site formed by the complementation of the nucleic acid and the oligonucleotide;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the cleavage being carried out using a restriction endonuclease that is active at the chosen temperature;

(iv) contacting the nucleic acid with a partially double-stranded oligonucleotide, the single-stranded region of the oligonucleotide being functionally complementary to the nucleic acids in the 5' terminal region that remains after the cleavage in step (iii) has been effected, and the double-stranded region of the oligonucleotide including any sequence necessary to return the sequences that remain after cleavage into proper and original reading frame for expression; and

(v) cleaving the nucleic acid solely at a restriction endonuclease cleavage site contained within the double-stranded region of the partially double-stranded oligonucleotide, the site being different from that used in step (iii) or amplifying the nucleic acid

using a primer at least in part functionally complementary to at least a part of the double-stranded region of the oligonucleotide, the primer introducing on amplification an endonuclease cleavage site and cleaving the amplified nucleic acid sequence solely at that site;

the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form, the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location, and the restriction being carried out using a cleavage endonuclease that is active at the chosen temperature; and

(vi) expressing a member of the family of peptides, polypeptides or proteins coded, at least in part, by the cleaved nucleic acids and collectively expressing at least a portion of the diversity of the family.

105. A library of immunoglobins comprising members having at least one variable domain in which one or both of the CDR 1 and CDR 2 have synthetic diversity and the CDR 3 has diversity captured from B-Cells.

106. The library according to claim 104, wherein a first variable domain has synthetic diversity in CDR 1 and CDR 2 and has diversity in CDR 3 captured from B-cells and a second variable domain has diversity captured from B-cells.

107. The library according to claim 104 or 105, wherein the variable domain is selected from the group of VH or VL.

108. A method for cleaving a nucleic acid sequence at a desired location, the method comprising the steps of:

(i) contacting a single-stranded nucleic acid sequence with a partially double-stranded oligonucleotide, the single-stranded region of the oligonucleotide being functionally complementary to the 5' terminal region of the nucleic acid sequence, the double-stranded region of the oligonucleotide including any sequences necessary to return the sequence in the single-stranded nucleic acid sequence into proper and original reading frame for expression; and

(ii) cleaving the partially double-stranded oligonucleotide-single-stranded nucleic acid combination solely at a restriction endonuclease cleavage site contained within the double-stranded oligonucleotide or amplifying the combination using a primer at least in part functionally complementary to at least part of the double-stranded region of the oligonucleotide, the primer introducing during amplification an endonuclease cleavage site and cleaving the amplified sequence solely at the site.

109. The method according to claim 108, wherein the length of the single-stranded portion of the partially double-stranded oligonucleotide is between 2 and 15 bases.

110. The method according to claim 109, wherein the length of the single-stranded portion of the partially double-stranded oligonucleotide is between 7 and 10 bases.

111. The method according to claim 108, wherein the length of the double-stranded portion of the partially double-stranded oligonucleotide is between 12 and 100 base pairs.

112. The method according to claim 111, wherein the length of the double-stranded portion of the partially double-stranded oligonucleotide is between 20 and 100 base pairs.

113. The methods according to any one of claims 99 to 104 and 108, further comprising at least one nucleic acid amplification step between one or more of steps (i) and (ii), steps (ii) and (iii), steps (iii) and (iv) and steps (iv) and (v).

114. A library comprising a collection of genetic packages that display a member of a diverse family of peptides, polypeptides or proteins and collectively display at least a portion of the diversity of the family, the library being produced using the methods of claims 99, 100, 103 or 113.

115. A library comprising a collection of members of a diverse family of peptides, polypeptides or proteins and collectively comprise at least a portion of the diversity of the family, the library being produced using the methods of claims 101, 102, 104 or 113.

116. The methods and libraries according to any one of claims 99 to 104 or 113, wherein the members of the library encode immunoglobulins.